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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/849,499	05/04/2001	Herman Waldmann	1324.028	8699

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EXAMINER
TON, THAIAN N

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 04/09/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/849,499	WALDMANN ET AL.	
	Examiner	Art Unit	
	Thai-An N. Ton	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *2/12/03* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *64-95 and 105-108* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *64-95 and 105-108* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *04 May 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicants' Amendment, filed 2/12/03, Paper No. 11, has been entered. Claims 64, 65, 69 and 70 have been amended. Claims 96-104 and 109 have been cancelled.

Claims 64-95 and 105-108 are under current examination.

Specification

The prior objection to the specification is maintained. Applicants have submitted a replacement specification that comprises the text of the parent published PCT reformatted in accordance with current USPTO practice. However, the substitute specification filed 2/12/03 has not been entered because it does not conform to 37 CFR 1.125(b) because: Applicants have not provided a copy of the specification excluding the claims, as well as a marked up version of the specification showing all the changes (including the matter being added to and the matter being deleted from) to the specification of record. See also MPEP §608.01(q).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The prior rejection of claims 64-95 and 105-108 under 35 U.S.C. 112, first paragraph, is *withdrawn* in view of Applicants' Affidavit, over the signature of the Attorney of Record, which confirms and verifies the deposit and the ultimate availability of the ESF116 mouse ES cell line to the public upon grant of a patent derived from the present application.

The prior rejection of claims 65-95 and 105-108 is *maintained* under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for producing a long-term culture of immature dendritic cells wherein the method comprises culturing ES cells from the mouse embryonic stem cell line ESF116 in the presence of murine IL-3 [and optionally, murine GM-CSF] to bring about differentiation of the ES cells into immature dendritic cells and stimulating the maturation of the immature dendritic cells with LPS, does not reasonably provide enablement for methods for producing long-term cultures of immature dendritic cells utilizing any population of ES cells, for the breadth claimed, culturing the ES cells in the presence of any cytokine or combination of cytokines to bring about the differentiation of the ES cells into immature dendritic cells to produce a long-term culture of immature dendritic cells, and stimulating the mature of the immature dendritic cells with any inflammatory mediator. The specification does not enable any person skilled in the art to which it pertains, or

with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Applicants argue that although the specification states that esDC may be generated from ES cells derived from some but not all mouse strains, this statement by the specification is based upon one failed attempt to differentiate the 129.Sv ES cell line, R1; and that the R1 cell line has been passed from laboratory to laboratory, the passage number has become excessively high, and as such, explains the present inventor's inability to achieve DC differentiation. Applicants argue that it is now common knowledge that other ES cell lines derived from 129/Sv mice are perfectly capable of supporting esDC growth. See p. 7 of the Response.

Applicants' arguments have been considered, however, they are not found to be persuasive. With regard to enablement, the specification must be enabling as of the filing date of the application. The statement by Applicants that it is *now* common knowledge that other ES cell lines are perfectly capable of supporting esDC growth does not provide enablement to the instantly claimed invention. MPEP §2164.05(a) states that:

> The state of the prior art is what one skilled in the art would have known, at the time the application was filed, about the subject matter to which the claimed invention pertains.
>
> The state of the prior art provides evidence for the degree of predictability in the art and is related to the amount of direction or guidance needed in the specification as filed to meet the enablement requirement. The state of the prior art is also related to the need for working examples in the specification.

The state of the art existing at the filing date of the application is used to determine whether a particular disclosure is enabling as of the filing date.

The specification fails to provide an enabling disclosure for utilizing any other ES cell line other than the ESF116 cell line, for the breadth claimed, to produce long-term cultures of immature dendritic cells. In fact, the specification supports that it would be unpredictable to utilize other ES cell lines [see p. 8, lines 19-28] in the claimed methods. Applicants have provided no teachings, guidance or evidence of record to overcome such unpredictability, and Applicants' statement that it is now be common knowledge that other ES cell lines would be capable of supporting esDC growth does not enable the instant invention at the time of filing.

Applicants further argue that two reasons why other laboratories culturing embryoid bodies with IL-3 and GM-CSF have not reported the production of DC; firstly that these groups are not skilled in the culture and study of DC, and that because the expertise of these investigators lay elsewhere, it would have been unlikely that the investigators would have had the background knowledge to identify DC in cultures. Secondly, Applicants argue that different cell types emerge from these cultures at different rates, and it is possible that the other investigators terminated their cultures before the DC had become the principle cell type. See pp. 7-8, bridging ¶.

Applicants have made unsubstantiated allegations without any documentation of record. Applicants' suggestion that previous investigators were not skilled, did not look for DC cells, or terminated their cultures before the DC

emerged do not provide support to enable the claimed invention. In particular, the specification must be enabling to persons of ordinary skill in the art, which would be considered other investigators culturing embryoid bodies.

Applicants argue that the prior Office action correctly points out that ES cells will not differentiate into DC in response to any cytokine/combination of cytokines, which is entirely unsurprising and expected. Applicants conclude that, "If every cytokine induced DC growth, the present invention would not be unexpected or surprising, which to the contrary, it is." See p. 8, 2nd full ¶.

It is noted that unexpected results, as discussed by Applicants are not used to overcome an enablement rejection, but an art rejection. In fact, Applicants' unexpected results lends support to the fact that culturing the mouse ES cell line ESF116 in the presence of murine IL-3 [and optionally, murine GM-CSF] would result in the production of immature dendritic cells.

Accordingly, in view of the quantity of experimentation necessary for the production of long-term cultures of immature dendritic cells by culturing any ES cells with any cytokine [or combination thereof], the lack of guidance, teachings and examples provided by the specification for the production of long-term cultures of immature dendritic cells from any ES cells with any cytokine, other than the exemplified ESF116 murine ES cell line with IL-3 [and optionally murine GM-CSF], as well as the unpredictable state of the art with regard to the availability of ES cells lines capable of supporting DC development, and the requirement for IL-3 for

differentiation, it would have required undue experimentation for one skilled in the art to make and/or use the claimed long-term cultures of dendritic cells and methods of making the same.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Thái-An N. Ton whose telephone number is (703) 305-1019. The examiner can normally be reached on Monday through Friday from 8:00 to 5:00 (Eastern Standard Time), with alternating Fridays off. Should the examiner be unavailable, inquiries should be directed to Deborah Reynolds, Supervisory Primary Examiner of Art Unit 1632, at (703) 305-4051. Any administrative or procedural questions should be directed to William Phillips, Patent Analyst, at (703) 305-3482. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 872-9306.

Deborah Crouch

TNT

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